PROC (BAYL UNIV MED CENT)
2022;35(3):403–404

https://doi.org/10.1080/08998280.2022.2039029

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ANTIFUNGAL COMBINATIONS IN MUCORMYCOSIS

Brigmon and colleagues reported the safety of long-term isavuconazole in a poorly controlled diabetic with rhinocerebral mucormycosis.[1] The authors diagnosed rhino-orbital mucormycosis and managed it with several antifungals, including liposomal amphotericin-B, intravenous micafungin, posaconazole, and finally isavuconazole. The index patient could have benefited from early surgery (partial or complete) since the drug penetration in the necrotic tissues (due to angioinvasion and thrombosis) is poor. Understandably, in the absence of surgical intervention, adding multiple antifungal agents failed to improve clinical status by day 11 of therapy.

Existing knowledge and current recommendations suggest surgery as the primary treatment for all forms of mucormycosis, including rhino-orbital and pulmonary mucormycosis.[2,3] The evidence for the combination of caspofungin with liposomal amphotericin is based on a retrospective study conducted over 12 years, comparing six patients receiving the combination therapy with 34 patients on monotherapy.[4] Further, the effect of caspofungin on the murine model of mucormycosis was demonstrated for *Rhizopus orzyae* (also known as *R. arrhizus)*. Mucorales are intrinsically resistant to echinocandins, except for *Rhizopus oryzae,* which has the *FKS* gene encoding for 1,3-β-glucan synthase (the target for echinocandins).[5] Whether *Rhizopus microsporus* (current case) would respond to a combination of caspofungin and liposomal amphotericin remains unknown.

While it is reassuring to note the safety of isavuconazole, there is no randomized trial evaluating the drug in mucormycosis, and the potential for QTc shortening needs to be remembered. The optimal duration of therapy is unknown, and the favorable response seen in the current case can be attributable to the control of diabetes mellitus. The role of optimizing blood sugars cannot be undermined, as mucormycosis has been shown to resolve spontaneously following diabetes control.[6] Thus, controlling the underlying medical condition and combined medical-surgical therapy are the cornerstone in managing mucormycosis.

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DR. EDWARD KRUSEN AND HIS CONTRIBUTIONS TO POLIO PATIENTS

Recent articles have discussed the contributions of William Beall Carrell, MD (1883–1944), and his son, Brandon Carrell, MD (1911–1981), both pediatric orthopedic surgeons, in serving children with polio and other musculoskeletal diseases in the Dallas area.[1–3] Within this context, I wanted to give credit to Dr. Edward M. Krusen (1929–2002) *(Figure 1)*, a physiatrist closely associated with Dr. Brandon Carrell who helped patients after their corrective surgeries to maximize function through rehabilitation. Dr. Krusen was also the first Muscular Dystrophy Association clinical director for the city of Dallas. The two formed a special bond and partnership in managing patients—so much so that a grateful patient made a large donation in their honor leading to the annual Carrell-Krusen Neuromuscular Symposium in Dallas, now in its 44th year.

As one of the few surviving retired physiatrists trained and mentored by Dr. Krusen, I have documented the history of the physical medicine and rehabilitation department at Baylor University Medical Center.[4] Dr. Edward M. Krusen and his physiatrist wife were recruited in 1950; he was chair at Baylor while Dr. Ursula became the chair at Parkland. Both were trained at Mayo Clinic in Minnesota by his uncle,

Figure 1. Dr. Edward Krusen.

Dr. Frank Krusen, author of the first textbook on physical medicine. At the end of Dr. Krusen's first year, he and his staff recorded a staggering 34,094 treatments. Among Dr. Krusen's first patients were 35 inpatients with polio. Patients were treated daily for several months in the Baylor Polio Convalescent Division, with outpatient therapy following for up to a year and a half.

On a personal note, I am very fortunate that Dr. Edward Krusen counted me as family. After Dr. Ursula died, he married Ruth. He and Ruth introduced me to the symphony and opera in Dallas, where they were patrons, and invited me into their home on Easter, Thanksgiving, and Christmas. Dr. Edward Krusen died in 2002.

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THE COLD DRINK HEART

A 56-year-old physician noted the onset of fast, irregular palpitations after ingestion of a few sips of a frozen margarita. He recognized the likely onset of atrial fibrillation, confirmed on an electrocardiogram, and self-treated it with aspirin and a beta-blocker. It resolved overnight. A subsequent medical workup, including thyroid function testing, an echocardiogram, and a treadmill stress test, were all normal.

In the ensuing years, there have been three subsequent similar episodes, all triggered by the ingestion of very cold substances. One happened immediately after several bites of an ice-cream cone, while biking on a hot summer day. Another occurred while drinking iced tea and eating sorbet. The last one happened during dessert (coffee ice cream over a meringue, with Kahlua added).

In view of this personal experience, the physician has alerted patients prone to paroxysmal atrial fibrillation to avoid ingestion of very cold substances. One, a middle-aged veteran jogger, had reported similar symptoms after a large glass of cold water following completion of a 10-km road race. An electrocardiogram documented atrial fibrillation, which resolved spontaneously after several hours.

The heart and the esophagus are in close proximity. Ingestion of very cold drinks or desserts can trigger paroxysmal atrial fibrillation and probably other arrhythmias. Patients should be notified as to the importance of avoiding such triggers.

When our index patient mentioned to his wife the various things that had stimulated his paroxysmal atrial fibrillation, her response was something like, "If you had half a brain you would avoid doing those things."

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